REMARKS

This Response is in reply to the Office Action dated January 10, 2006. Claims 6, 23-25, 31-35, 39-44, 46, 48-52, 54-56, 58-64, 66-67, 69-77 are pending in the application. Claims 1-5, 7-22, 26-30, 36-38, 45, 47, 53, 57, 65, 68 and 78-80 are canceled. All of the claims currently stand rejected under 35 U.S.C. §§ 112, 102 and 103. Claims 6, 23, 31, 42, 44, 46, 50, 51, 56, 64, 67, 72, 73 and 76 have been amended.

Independent Claim 6 has been amended to clarify that the cell culture includes a human neural precursor cell line. Support for the term "human" can be found at page 10 in the first sentence of the last paragraph. Independent Claims 6, 23, 31, 51, 64 and 72 have been amended to clarify that the cells or cell line of the invention resist differentiation in media containing a mitogen. Support for the amendment can be found on page 10 in the last sentence of the first paragraph and the second sentence of the last paragraph and the related disclosed methods.

In the Office Action, Claims 6, 23-25, 31-35 and 39-77 were rejected under 35 U.S.C. §112, second paragraph, as failing to comply with the written description requirement.

The phrase "wherein at least about 20% of the cell line is capable of differentiating into neurons upon withdrawl of mitogen" as found in claims 6, 23 and 51 was rejected as not meeting the written description requirement. Applicants submit that adequate support for this phrase can be found in the specification in the first paragraph of page 19. Where after 10 days neuron markers are found on differentiated cells at 50% for early markers, and 20%-30% for mature markers. In addition, the paragraph beginning at the bottom of page 25 teaches the interchangeability of ligand binding domains such as glucocorticoid receptor, progesterone receptor ligand binding domain which was described as being particularly suitable MycPR, androgen receptors, etc. Nevertheless, the "20%" language has been removed from the claims and replaced with the phrase "a portion" in claim 51 and "said cell line" in claim 6. Applicant submits that the recited passages support this language in the claims.

The phrase ""wherein the c-myc construct *includes at least a portion of a* c-myc *DNA* (versus the c-myc cDNA)... encoding *at least a portion of*" a ligand binding domain"" as found in claims 1, 23 and 51 was rejected as not meeting the written description requirement. Applicants submit that adequate support for this phrase can be found in the specification in

Figure 1, which illustrates the c-myc construct and in the description of the example on page 11 in which the c-myc construct which describes the use of the EcoR1 fragment of the c-myc cDNA fusion with the estrogen receptor cDNA. The Eilers reference describes the construct as encompassing exons 2 and 3 of the genomic DNA for myc and indicates that nucleotides 282-576 from the ligand binding domain are included It is submitted that one of skill would appreciate that these descriptions represent portions of the respective genes. Nevertheless, the language found objectionable, "*at least a portion of,*" has been deleted from claim 31 and 51.

Claims that do not require the first and second mitogens to be different were rejected as not meeting the written description requirement. Applicant submits that the specification supports both aspects, for example, at page 15 which describes studies in which bFGF was used as a sole mitogen and growth rates compared to cultures grown with a combination of mitogens. Thus, Applicant respectfully submits that claim language directed to the use of first and second mitogens that are the same or different are both supported by the specification.

The term "proto-oncogene" in Claim 72 was rejected as not meeting the written description requirement. Applicant disagrees with the rejection as the term proto-oncogene is well known and is, in fact, used in the specification at page 10 in the last sentence of the middle paragraph. Other examples of suitable proto-oncogenes are also described beginning at the bottom of page 25 and continuing through the end of page 27. In order to advance prosecution, Claim 72 has been amended to substitute the phrase "c-myc DNA" for this term. Applicant in no way intends for this amendment to be construed as acquiescence in the rejection.

The phrase "differentiate into... *glial*" was rejected as not meeting the written description requirement. Support for this phrase can be found on page 19 in the last line and in the second complete paragraph on page 20.

The phrase, "wherein the culture includes a monolayer (versus feeder) component" was rejected as not meeting the written description requirement. Although Applicant disagrees with the rejection and does not intend to acquiesce in the rejection, Applicant is canceling the relevant claims (Claims 39, 45, 47, 57 and 68) without prejudice in order to advance prosecution of this case.

The phrase "tissue selected from the group consisting of ... *diencephalon, mesencephalon,..*" was rejected as not meeting the written description requirement. Although Applicant disagrees with the rejection because one of skill would certainly understand that the mesencephalon and diencephalon terms are regions of the brain and a potential source of stem cells, Applicant is canceling the relevant language in these claims (Claims 42, 56, 67 and 76) without prejudice in order to advance prosecution of this case. Applicant in no way intends for cancellation of these elements to be construed as an acquiescence in the rejection.

The phrase "wherein the neural precursor cell is derived from an *adult* human" was rejected as not meeting the written description requirement. Although Applicant disagrees with the rejection because one of skill would certainly understand that an adult human could serve as a source of stem cells. Applicant is canceling the relevant claim (Claim 53) without prejudice in order to advance prosecution of this case. Applicant in no way intends for cancellation of this claim to be construed as an acquiescence in the rejection.

The phrase "further comprising culturing the neural precursor cells in the presence of *unmodified* cells..." was rejected as not meeting the written description requirement. Claims 62 and 63 have been amended to clarify that the neural precursor cells can be grown in the presence of feeder cells. Support for this phrase can be found in the two paragraphs that begin on page 14 which describes the use of feeder cells.

The phrase "a neural precursor cell line.. capable of *expanding through at least thirty cell doublings*" was rejected as not meeting the written description requirement. Support for this phrase can be found on page 24 where the specification states "Thus, our objective has been to increase the expansion capacity well beyond the 30 cell doublings at least up to the beginning of senescence which is thought to occur between 60 and 80 cell cycles" and on page 3 where the specification states "Although the 30 cell-doublings yield 10^9-fold expansion of cells, a method for further significant expansion of CNS stem cells would be of significant commercial value. Here, we disclose that constitutive activation of c-myc protein in CNS stem cells prevents their spontaneous differentiation at high cell density, confers resistance to glial differentiation, and increases the mitotic capacity over 60 cell-doublings."

The phrase "wherein the neural precursor cell line *includes a neural stem cell line"* was rejected as not meeting the written description requirement. Although Applicant disagrees with the rejection and does not intend to acquiesce in the rejection, Applicant is canceling the relevant claim (Claim 65) without prejudice in order to advance prosecution of this case.

The phrase "includes *a clonal cell culture"* was rejected as not meeting the written description requirement. Claims 44 and 46 have been amended to clarify that the cultures contain a clonal cell line. This phrase finds support on page 14 which describes the growth of individual clones and clonal expansion techniques which would clearly result in a clonal cell line.

In contrast to the position taken in the Office Action on page 4, the specification contains a complete teaching of an expressed c-myc-estrogen receptor fusion protein gene in a retrovirus. Beginning in the Example on page 11 and by reference to figure 1. All the sequences involved are known and can readily be discerned from the present disclosure by one of skill in the art and by reference to Eiler et al., Nature (1988) 340, 60, as described in more detail above.

Applicant has made an earnest effort to address each of the 35 U.S.C. § 112 issues raised in the Office Action and believes the pending claims are all adequately supported by the specification and requests that the rejections be withdrawn.

In the Office Action, Claims 6, 23, 25, 31, 33-35, 39-51 and 54-77 stand rejected under 35 U.S.C. § 102(b) as being anticipated by *Nakafuku et al.* ("*Nakafuku*"). Applicants respectfully traverse these rejections for at least the reasons discussed below.

Of the rejected claims, Claims 6, 23, 31, 51, 64 and 72 are independent. These claims have been amended to clarify that the respective claimed cells and cell lines resist differentiation when grown in medium containing a mitogen. This is quite unlike the cells in *Nakafuku* which, as the Office Action acknowledges, differentiate most efficiently in the presence of mitogens. (Page 163, column 1) As stated in *Nakafuku*, differentiation of MNS-57 cells can be conditionally induced in response to exogenous stimuli, which is, in this case, the combination of bFGF and c-*myc* activation by estrogen. (Page 163, column 2) These factors appear to be important for maximal differentiation of MNS-57 cells. Thus, it simply cannot be said that the *Nakafuku* cells resist differentiation when grown in medium containing mitogen, as required by

the present independent claims. Moreover, with respect to Claim 6, *Nakafuku* does not disclose stable human progenitor cells, as required by that claim. For these reasons independent Claims 6, 23, 31, 51, 64 and 72 exclude *Nakafuku* and Applicants request that the rejections under 35 U.S.C. § 102 be reconsidered and withdrawn. Moreover, *Nakafuku* teaches away from the use of mitogens, such as estradiol and bFGF, in the maintenance of stable neural precursor cells since such conditions maximize differentiation of the *Nakafuku* cells. Therefore, *Nakafuku* simply cannot make the claimed cells and methods obvious.

Further, nothing in the teachings of *Eilers* or *Evans* can remedy the deficiencies in *Nakafuku* with respect to the present rejection for obviousness since, at most, the references could only provide contradictory teachings with respect to stimulating differentiation. Such teachings, even if they were present (which Applicant submits is not the case), would still not make the cells, cell lines or methods of the present claims obvious, as the net result would only be conflicting teachings with respect to differentiation stimuli. Moreover, *Eilers* contains no teaching with respect to differentiation and only demonstrates estrogen-dependent growth stimulation with its *mycer* constructs. *Evans* fails to teach or suggest mammalian neural precursor cells comprising a proto-oncogene and, therefore, has little to say about the conditions under which such cells would resist differentiation or how they could be efficiently induced to differentiate. *Evans* fails to provide any clear indication of how hormones would affect any given cell line or construct and thus, even when combined with *Nakafuku*, fails to render the present claims which require cells or cell lines and related methods that resist differentiation in the presence of mitogens obvious. Accordingly, the combination of *Nakafuku*, *Eilers* and *Evans* fails to teach or suggest every element of the claimed invention.

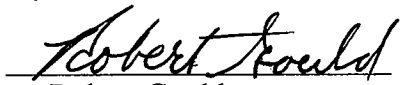
Applicants respectfully submit that independent Claims 6, 23, 31, 51, 64 and 72 are patentable over the combination of *Nakafuku*, *Eilers* and *Evans* and request that the rejection be reconsidered and withdrawn.

Applicants respectfully submit that independent Claims 6, 23, 31, 51, 64 and 72 are suitable for allowance. Further, Applicants submit that their dependent Claims 24, 25, 32-35, 39-44, 46, 48-50, 52, 54-56, 58-63, 66, 67, 69-71, and 73-77 are also allowable as these claims contain all of the limitations of their independent base claims.

An earnest endeavor has been made to place this application in condition for allowance and such allowance is courteously solicited. Please charge Deposit Account No. 02-1818 for any insufficiency or credit the account for any overpayment. If the Examiner has any questions related to this Response, Applicants respectfully submit that the Examiner contact the undersigned.

Respectfully submitted,

BELL, BOYD & LLOYD LLC

BY 

Robert Gould
Reg. No. 43,642
Customer No. 24573

Dated: May 19, 2006